

255159
RECORD NUMBER

1/11/90

031301
SHAUGHNESSEY NO.

REVIEW NUMBER

ECOLOGICAL EFFECTS BRANCH REVIEW

DATE: IN 11-27-89 OUT _____

FILE OR REG. NO. 45639-128

PETITION OR EXP NO. _____

DATE OF SUBMISSION 4-12-88

DATE RECEIVED BY EFED 11-20-89

RD REQUESTED COMPLETION DATE 1-20-90

EEB ESTIMATED COMPLETION DATE 1-20-90

RD ACTION CODE/TYPE OF REVIEW 660

TYPE PRODUCT(S): I, D, H, F, N, R, S Fungicide

DATA ACCESSION NO(S). 405831-03

PRODUCT MANAGER NO. E. Feris (74)

PRODUCT NAME(S) Dichloran

COMPANY NAME Nor-Am Chemical Company

SUBMISSION PURPOSE Submission of avian acute oral LD₅₀
(Mallard) in response to RS

SHAUGHNESSEY NO.	CHEMICAL AND FORMULATION	% A.I.
_____	_____	_____
_____	_____	_____
_____	_____	_____

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Memorandum

Subject: Review of an Avian Single-Dose Oral LD₅₀ Toxicity Test
(Mallard) for Dichloran Technical (DCNA)
(Accession No. 405831-03)

From: 
James W. Akerman, Chief
Ecological Effects Branch
Environmental Fate And Effects Division (H7507C)

To: Eric Feris (PM-74)
Reregistration Branch
Special Review/Reregistration Division (H7508C)

Attached is the Ecological Effects Branch review of an avian single-dose oral LD₅₀ toxicity test on the mallard duck for Dichloran Technical (DCNA).

The methods used in conducting this study were not in accordance with procedures specified in Section 71-1 of the Environmental Protection Agency Pesticide Assessment Guidelines Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms. The study did not provide useful information and, therefore, is not acceptable for use in a risk assessment. The authors failed to establish that the avian single-dose oral LD₅₀ is greater than 2000 mg/kg, or establish a valid LD₅₀ value with corresponding 95 percent confidence intervals. The "split-dosing" procedure used in this study is inconsistent with other comparable acute toxicity testing methods and, therefore, cannot be considered as a reliable means for comparing the toxicity of Dichloran Technical to other compounds.

This study should be conducted using northern bobwhite quail or another gallinaceous bird species to verify if the compound produces a similar emetic response. In addition, a different method could be used to administer the compound such as gelatin capsules. It is recommended that an avian dietary LC₅₀ test be conducted using the technical grade material to compare the results with the LD₅₀ test. This information will aid in determining food consumption and also serve as a useful palatability study of the subject compound.

DATA EVALUATION RECORD

1. **CHEMICAL:** DCNA
2. **TEST MATERIAL:** Technical Dichloran (97.5% a.i.), a yellow powder
3. **STUDY TYPE:** Avian Single-Dose Oral LD₅₀
Species Tested: Mallard Duck (Anas platyrhynchos)

4. **STUDY IDENTIFICATION:**

Author(s): Roberts, N.L., and C. Phillips
Laboratory: Huntingdon Research Centre.
Huntington, Cambridgeshire
England

Study No.: TOX 87225


Study Date: March 16, 1989

Submitted By: Nor-AM Chemical Company

Accession No: 405831-03

5. **REVIEWED BY:**

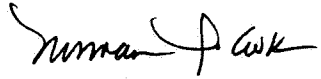
Art Roybal
Wildlife Biologist
Ecological Effects Branch, EFED

Signature: 

Date: 1-12-90

6. **APPROVED BY:**

Norman Cook
Supervisory Biologist
Ecological Effects Branch, EFED

Signature: 

Date: 1-11-90

7. **CONCLUSIONS:** The methods used in conducting this study were not in accordance with procedures specified in Section 71-1 of the Environmental Protection Agency Pesticide Assessment Guidelines Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms. The study did not provide useful information and, therefore, is not acceptable for use in a risk assessment. The authors failed to establish that the avian single-dose oral LD₅₀ is greater than 2000 mg/kg, or establish a valid LD₅₀ value with corresponding 95 percent confidence intervals. The "split-dosing" procedure used in this study is inconsistent with other comparable acute toxicity testing methods and, therefore, cannot be considered as a reliable means for comparing the toxicity of Dichloran Technical to other compounds.

8. RECOMMENDATIONS: N/A
9. BACKGROUND: N/A
10. DISCUSSION OF INDIVIDUAL TESTS: N/A
11. MATERIALS AND METHODS:

A. Test Animals: All bobwhite quail (Colinus virginianus) were over 16 weeks of age and ranged in weight from 895 to 1250 grams at pre-treatment acclimation. The birds were obtained from Mr. J. Coles, County Game Farm, Home Farm, Hothfield, Ashford, Kent. Birds were identified by a numbered metal wing tag.

B. Test Conditions: Test birds were housed in groups of five according to sex and treatment. The pens used for holding the birds were constructed from galvanized steel and wire mesh with a raised wire mesh floor. Each pen, measuring approximately 1.5 X 1.2 m, contained a galvanized steel food hopper and an automatic drinker. The pens were in a building which provided appropriate environmental conditions for the species. Ventilation fans were adjusted as necessary and a controlled artificial lighting pattern of 7 hours light and 17 hours darkness was followed. The housing facilities ambient temperature ranged between 17 and 20°C. Water and feed were provided ad libitum during acclimation and the test.

C. Treatment:

Range-finding: The author's determined dose levels for the main study by using pairs of birds dosed by oral intubation with Dicloran suspended in corn oil. Two birds (one female and one male) were given a single dose of 2000 mg/kg at a rate of 5 ml/kg (dose concentration 40% w/v). The following morning (19 hours after dosing) signs of vomit were observed on the sides and floor of the pen. Subsequently, two additional birds were dosed at the same dose level using a dose of half the concentration at a rate of 10 ml/kg. No vomiting or other clinical signs of toxicity were observed.

Treatment Groups: Phase I - The birds were weighed and wing-tagged fourteen days prior to dosing and were arbitrarily allocated to treatment groups of ten (five males and five females). Nominal concentration levels used in Phase I of this study were 625, 1250, and 2500 mg/kg. Test and control birds were dosed by oral intubation at a rate of 10 ml/kg administered as a single dose. One operator held each bird's beak open while another operator administered

the syringe. Care was taken to ensure that the bird had ingested all the dose material before being returned to its pen. Within fifteen minutes following dosing, all test birds vomited.

Phase II - The author's then decided to dose additional groups of birds using a "split-dosing" procedure where half of the total dose was administered in the morning and the other half in the afternoon of the same day. Fifty birds were used in groups of ten containing 5 females and 5 males. Nominal concentration levels used in Phase II were 313 (156.5 a.m./p.m.), 625 (312.5 a.m./p.m.), 1250 (625 a.m./p.m.), and 2500 (1250 a.m./p.m.) mg/kg. After the initial (a.m.) dose, birds in the 625, 1250, and 2500 mg/kg groups vomited within approximately half an hour after dosing. No clinical signs were observed initially at the 313 mg/kg dose level, but within approximately one and threequarter hours following dosing, signs of vomit were observed on the birds and on the walls and floor of the pen. At this point in the study the author's stated, "Since the compound had emetic effects at all dose levels after the initial dose, the study was terminated."

Phase III - Forty additional birds were allocated to treatment groups of 5 males and 5 females. A "split-dosing" procedure was followed as before using the following dose concentrations: 40 (20 a.m./p.m.), 79 (39.5 a.m./p.m.), 157 (78.5 a.m./p.m.).

D. Observation Period: For the main study there was a 14-day pre-treatment acclimation period followed by a 14-day post-treatment observation period after dosing. Mortality and clinical observations were made daily. Individual bodyweights were taken 14 and 7 days before the birds were dosed. In addition, bodyweights were measured immediately before dosing and at Day 7 and Day 14 after dosing.

E. Statistics: The mortality pattern in this study does not allow for the calculation of the median lethal dose value.

2. REPORTED TEST RESULTS:

Observations: Phase III - There were no signs of vomiting and no mortalities in any birds following dosing. Within forty-five minutes after the first dose, a number of birds in the 157 mg/kg passed excreta containing yellowish material resembling the test substance. No clinical signs were observed following the second dose and all birds remained in good health throughout the post-treatment period.

Necropsy: No macroscopic abnormalities were found in any of the birds examined.

Body Weights and Feed Consumption: Individual bodyweights are given in Appendix I and group mean body weights are summarized in Table 1. The author's considered bodyweight changes variable but within normal limits in all treatment groups. A summary of group mean food consumption results is given in Table 2.

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:

"The acute oral toxicity (LD_{50}) of technical dicloran, suspended in corn oil and administered by intubation as two equal doses on one day, was in excess of 157 mg/kg, the high non-emetic dose level."

The study was conducted so as to conform with Good Laboratory Practices as published by the U.S. Environmental Protection Agency, Office of Pesticide Programs in 40 CFR Part 160.

14. REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS:

A. Test Procedure: The methods used in conducting this study were not in accordance with procedures specified in Section 71-1 of the Environmental Protection Agency Pesticide Assessment Guidelines Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms. The following detract from the study's soundness and usefulness in a risk assessment:

- o The authors failed to establish that the avian single-dose oral LD_{50} is greater than 2000 mg/kg, or establish a valid LD_{50} value with corresponding 95 percent confidence intervals. The "split-dosing" procedure used in this study is inconsistent with other comparable acute toxicity testing methods and, therefore, cannot be considered as a reliable means for comparing the toxicity of Dichloran Technical to other compounds. In a median lethal dose test, the entire dosage should be administered as a single dose not as two equal doses with a lengthy time interval between dosages. The "split-dosing" procedure can be very misleading in that the first dosage administered in the morning can enhance the birds' tolerance to the afternoon dosage.

This study should be conducted using northern bobwhite quail or another gallinaceous bird species to verify if administration of the compound results in a similar emetic response. In addition, a different method could be used to administer the compound such as gelatin capsules. It is recommended that an avian dietary LC_{50}

test be conducted using the technical grade to compare the results with the LD₅₀ test. This information will aid in determining food consumption and also serve as a useful palatability study of the subject compound.

- o The authors did not specify how long the birds were fasted prior to dosing. Feed should be withheld from all birds for at least 15 hours prior to oral dosing.
 - o A 7 hours light and 17 hours darkness photoperiod was followed. (The EPA SEP recommends a photoperiod of 10 hours light and 14 hours darkness.)
- B. Statistical Analysis: There were no mortalities from the study. A statistical analysis was not feasible.
- C. Discussion/Results: See above Test Procedure discussion.
- D. Adequacy of the Study:
- (1) Classification: Invalid
 - (2) Rationale: The study provided no useful information. The study deviated significantly from recommended protocols and, therefore, will not be useful in a risk assessment.
 - (3) Repairability: See above Test Procedure Discussion
15. REFERENCES: Hill, Elwood. 1989. Personal Communication on December 14, 1989. U.S. Fish and Wildlife Service. Patuxent Wildlife Research Center, Wildlife Toxicology.
16. Completion of One-Liner: Yes, on 12/18/89

Shaughnessy No. 031301

(DCNA)

Chemical Name Dichloraz

Chemical Class _____

Page 1 of _____

Study/Species/Lab/

Chemical s.a.i

14-Day Single Dose Oral LD50

Species: Mallard

Lab.: Huntingdon Res Centre

Acc. #: 405831-03

LD50 >157 mg/kg (95% C.L.)

Slope = N/A # Animals/Level = 10

Results
Contr. Mort. (%) = 0

Reviewer/Date
Validation Status

Age (Days) = +16 weeks

Sex = ♀♂ Royal Invalid
12/18/89

14-Day Dose Level mg/kg/(% Mortality)

Comments: 40 (0%), 79 (0%), 157 (0%),
No Mortality - 1/2 dosage / 1/2 dosage - a.m. & p.m. dosages - "Split-closing" procedure

14-Day Single Dose Oral LD50

Species:

Lab.:

Acc. #:

LD50 = mg/kg (95% C.L.)

Slope = # Animals/Level =

Contr. Mort. (%) =

Age (Days) =
Sex =

14-Day Dose Level mg/kg/(% Mortality)

Comments:

8-Day Dietary LC50

Species

Lab.:

Acc. #

LC50 = ppm (95% C.L.)

Slope = # Animals/Level =

Contr. Mort. (%) =

Age (Days) =
Sex =

8-Day Dose Level ppm/(% Mortality)

Comments:

8-Day Dietary LC50

Species:

Lab:

Acc. #

LC50 = ppm (95% C.L.)

Slope = # Animals/Level =

Contr. Mort. (%) =

Age (Days) =
Sex =

8-Day Dose Level ppm/(% Mortality)

Comments:

96-hour LC50

Species:

Lab:

Acc. #:

LC50 = PP (95% C.L.)

Slope = # Animals/Level =

Contr. Mort. (%) =
Sol. Contr. Mort. (%) =

Temperature =

96-Hour Dose Level pp/(% Mortality)

Comments:

96-hour LC50

Species:

Lab.:

Acc. #:

LC50 = PP (95% C.L.)

Slope = # Animals/Level =

Con. Mor. (%) =
Sol. Con. Mor. (%) =

Temp. =

96-Hour Dose Level pp/(% Mortality)

Comments:

96-hour Invertebrate

Species:

Lab.:

Acc. #:

LC50 = PP (95% C.L.)

Slope = # Animals/Level =

Con. Mort. (%) =
Sol. Con. Mort. (%) =

Temp. =

96-Hour Dose Level pp/(% Mortality)

Comments:

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Study/Species/Lab/ Accession #	Chemical & Active	Results				Reviewer/ Date	Validation Status
		Group	Dose(ppm)	Effectuated/Parameters	Mort.(%)		
Avian Reproduction,		Control	_____	_____	_____		
Species:		Treatment I	_____	_____	_____		
Lab:		Treatment II	_____	_____	_____		
Acc. #:		Treatment III	_____	_____	_____		
		Study Duration:					
		Comments:					

Field Study(Simulated/Actual)	Group	Rate(ai/a)	Treatment Interval	Total # Treatments	Mor.(%)		
Species:	Control	_____	_____	_____	_____		
	Treatment I	_____	_____	_____	_____		
Lab:	Treatment II	_____	_____	_____	_____		
Acc. #:	Treatment III	_____	_____	_____	_____		
		Crop/Site:	Study Duration:				
		Comments:					

Chronic fish,

Species _____ Concentrations Tested (pp_) = _____

MAIC = > _____ < _____ PP _____ Effectuated Parameter = _____

Lab: _____ Contr. Mort.(%) = _____ Sol. Contr. Mort.(%) = _____

Acc. #: _____ Comments: _____

Chronic invertebrate,

Species _____ Concentrations Tested (pp_) = _____

MAIC => _____ < _____ PP _____ Effectuated Parameter(s) _____

Lab: _____ Contr. Mort.(%) = _____ Sol. Contr. Mort.(%) = _____

Acc. #: _____ Comments: _____

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Use this form for individual studies & to submit pesticide applications.



United States Environmental Protection Agency
Office of Pesticide Programs
Washington, DC 20460
Data Review Record
Confidential Business Information - Does not contain
National Security Information (E.O. 12065)

Pack Number
49843
EFED

Date Received
11-20-89

1. Product Name <i>W44 Technical Dichloran</i>					Chemical Name <i>DCNA</i>		
2. Identifying Number <i>45639-128</i>	3. Record Number <i>255159</i>	4. Action Code <i>660</i>	5. MRID/ Accession Number <i>40583103</i>	6. Study Guideline or Narrative <i>71-1</i>			
7. Reference No.	8. Date Rec'd (EPA) <i>4-12-88</i>	9. Prod/Review Mgr/DCI <i>E.FELAS</i>	10. PM/RM Team No. <i>74</i>	11. Date to HED/EFED/RD/BEAD <i>11-20-89</i>	12. Proj Return Date <i>1-20-90</i>	13. Date Returned to RD/SRRD	

Instructions
Please review data

031301/0113

This Section Applies to Review of Studies Only

14. Check Applicable Box				15. No. of Individual Studies Submitted	
<input type="checkbox"/> Adverse 6(a)(2) Data (405)	<input checked="" type="checkbox"/> Generic Data (Reregistration)(660)	<input type="checkbox"/> Product Specific Data (Reregistration)(655)		1	
16. Have any of the above studies (in whole or in part) been previously submitted for review?				17. Related Actions	
<input type="checkbox"/> Yes (Please identify the study(ies))				<input type="checkbox"/> No	
18.	To	Type of Review	19. Reviews Also Sent to		20. Data Review Criteria
HED		Science Analysis & Coordination	<input type="checkbox"/> SAC	<input type="checkbox"/> PC	A. Policy Note No. 31 <input type="checkbox"/> 1 = data which meet 6(a)(2) or meet 3(c)(2)(B) flagging criteria <input type="checkbox"/> 2 = data of particular concern from registration standard <input type="checkbox"/> 3 = data necessary to determine tiered testing requirements
		Toxicology/HFA	<input type="checkbox"/> TOX/HFA	<input type="checkbox"/> PL	
		Toxicology/IR	<input type="checkbox"/> TOX/IR	<input type="checkbox"/> EA	
		Dietary Exposure	<input type="checkbox"/> DEB	<input type="checkbox"/> AC	
EFED	<input checked="" type="checkbox"/>	Ecological Effects	<input type="checkbox"/> NDE	<input type="checkbox"/> BA	B. Section 18 <input type="checkbox"/> 1 = data in support of section 3 in lieu of section 18 C. Inert Ingredients <input type="checkbox"/> 1 = data in support of continued use of List 1 inert
		Environmental Fate & Groundwater	<input type="checkbox"/> EEB		
SRRD		Special Review	<input type="checkbox"/> EFGWB		
		Reregistration	<input type="checkbox"/> SR		
		Generic Chemical Support	<input type="checkbox"/> RER		
RD		Insecticide-Rodenticide	<input type="checkbox"/> GSC		
		Fungicide-Herbicide	<input type="checkbox"/> IR		
		Antimicrobial	<input type="checkbox"/> FH		
		Product Chemistry	<input type="checkbox"/> AM		
BEAD		Precautionary Labeling			
		Economic Analysis			
		Analytical Chemistry			
		Biological Analysis			

Confidential Statement of Formula (EPA Form 8570-4) Attached (Trade Secrets) Label Attached



United States Environmental Protection Agency
Office of Pesticide Programs
Washington, DC 20460

Data Review Record

Confidential Business Information - Does not contain
National Security Information (E.O. 12065)

Pack Number

49843
EFED

Date Received

11-20-89

1. Product Name: W44 Technical Dichloran
Chemical Name: DCNA

2. Identifying Number	3. Record Number	4. Action Code	5. MRID/ Accession Number	6. Study Guideline or Narrative
45639-128	255159	660	40593103	71-1

7. Reference No. 8. Date Rec'd (EPA) 9. Prod/Review Mgr/DCI 10. PM/RM Team No. 11. Date to HED/EFED/RD/BEAD 12. Proj Return Date 13. Date Returned to RD/SRRD

4-12-88 E.F. RAS 74 11-20-89 1-20-90

Instructions

Please review data

031301/0113

This Section Applies to Review of Studies Only

14. Check Applicable Box: 3

Adverse 6(a)(2) Data (405)
 Special Review Data (870)
 Generic Data (Reregistration) (660)
 Product Specific Data (Reregistration) (655)

15. No. of Individual Studies Submitted: 1

16. Have any of the above studies (in whole or in part) been previously submitted for review?
 Yes (Please identify the study(ies)) No

17. Related Actions

18.	To	Type of Review	19. Reviews Also Sent to	20. Data Review Criteria
HED		Science Analysis & Coordination	<input type="checkbox"/> SAC <input type="checkbox"/> PC	A. Policy Note No. 31 <input type="checkbox"/> 1 = data which meet 6(a)(2) or meet 3(c)(2)(B) flagging criteria <input type="checkbox"/> 2 = data of particular concern from registration standard <input type="checkbox"/> 3 = data necessary to determine tiered testing requirements B. Section 18 <input type="checkbox"/> 1 = data in support of section 3 in lieu of section 18 C. Inert Ingredients <input type="checkbox"/> 1 = data in support of continued use of List 1 inert
		Toxicology/HFA	<input type="checkbox"/> TOX/HFA <input type="checkbox"/> PL	
		Toxicology/IR	<input type="checkbox"/> TOX/IR	
		Dietary Exposure	<input type="checkbox"/> DEB <input type="checkbox"/> EA	
		Nondietary Exposure	<input type="checkbox"/> NDE <input type="checkbox"/> AC	
EFED	<input checked="" type="checkbox"/>	Ecological Effects	<input type="checkbox"/> EEB <input type="checkbox"/> BA	
		Environmental Fate & Groundwater	<input type="checkbox"/> EFGWB	
SRRD		Special Review	<input type="checkbox"/> SR	
		Reregistration	<input type="checkbox"/> RER	
		Generic Chemical Support	<input type="checkbox"/> GSC	
RD		Insecticide-Rodenticide	<input type="checkbox"/> IR	
		Fungicide-Herbicide	<input type="checkbox"/> FH	
		Antimicrobial	<input type="checkbox"/> AM	
		Product Chemistry		
		Precautionary Labeling		
BEAD		Economic Analysis		
		Analytical Chemistry		
		Biological Analysis		

Confidential Statement of Formula (EPA Form 8570-4) Attached (Trade Secrets) Label Attached